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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,281	06/09/2005	Jean-Christophe Leroux	1017753-000204	4230

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
03/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/507,281	LEROUX ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-15,20,21,23,26,27,30-35 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-15,20,21,23,26,27,30-35 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks, amendments, and Request for Continued Examination filed on 11/17/08 are acknowledged.

2. Claims 2, 16-19, 22, 24-25, 28-29, and 36-37 were cancelled. Claims 1, 4, 5, 13, 14, 30, 31, and 38 were amended.

3. Claims 1, 3-15, 20-21, 23, 26-27, 30-35, and 38 are included in the prosecution.

Continued Examination under 37 CFR 1.114

4. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/17/08 has been entered.

Response to Arguments

Rejection of claims 1, 3-16, 20-21, 23, 26-27, and 29-38 under 35 USC § 103(a)

5. Applicant's arguments, see Page 9, filed 11/17/08, with respect to the rejection of claims 1, 3-16, 20-21, 23, 26-27, and 29-38 under 35 USC § 103(a) as being unpatentable over Fanara et al. (US 6,464,987) in view of El Nokaly et al. (US 5,843,407) have been fully considered but are not found persuasive.

Applicant argues that Fanara does not teach any organogelling substance which is an amino acid derivative, much less one of the four specific compounds LAM, LAE, SAM and SAE.

This is not persuasive because Fanara teaches compositions that have the property of gelling upon contact with mucous membranes (Col. 1, line 65 to Col. 2, line 5) and El-Nokaly, the supporting reference, teaches n-acyl amino esters as suitable gelling agents (Col. 5, lines 10-14).

Applicant argues that Fanara's compositions are not heat sensitive and that Fanara's compositions will not have a transition temperature from liquid to gel lower than the temperature of the site of the injection. Applicant argues that Fanara teaches in column 5, lines 18-26, that their compositions gel instantaneously in the presence of an aqueous phase; and that this does not evidence sensitivity to heat.

This is not persuasive because Fanara teaches compositions that are fluid (Col. 5, lines 18-20) and that a gel forms under the skin or in the muscle (Col. 1, line 65 to Col. 2, line 5).

Applicant argues that the elements of the amino acid derivatives LAM, LAE, SAM or SAE are not described or even suggested by El-Nokaly.

This is not persuasive because El-Nokaly teaches the compatibility of the n- acyl amino acid esters with plant oils, which meets the limitation of an organogelling substance and a hydrophobic organic liquid. When combined with Fanara, the gelling substance of El-Nokaly can be used for in-vivo administration. Fanara's composition is

fluid and forms a gel under the skin or in muscle, and allows the sustained release of at least one active substance.

Applicant argues that the El-Nokaly patent relates to lipstick compositions which comprise a gelling agent and that the El-Nokaly patent neither discloses nor suggests any specific alanine ester derivatives, much less these four compounds.

This is not persuasive because El-Nokaly teaches n-acyl amino acid esters that are suitable gelling agents and one of ordinary skill in the art would find the specific amino acid derivatives, LAM, LAE, SAM, and SAE, obvious variants of the broad group of n-acyl amino acid esters. It would have been obvious to one of ordinary skill in the art at the time the invention was made to choose from a finite number of predictable n-acyl amino acid esters as gelling agents with a reasonable expectation of success of producing a functional product with an organogelling substance.

Applicant argues that the presence of amino acid derivatives in a lipstick composition does not mean that it is safe to be incorporated in a composition dedicated to be administered *in vivo* by injection.

This is not persuasive because one of ordinary skill in the art would find it obvious to include only pharmaceutical grade material (including the amino acid esters taught by El-Nokaly) in a composition that is intended for administration as a subcutaneous or intramuscular injection. One of ordinary skill in the art would follow the current good manufacturing practices required by the pharmaceutical production facility for producing materials that will be injected into a body.

Applicant argues that it is not taught or suggested by El-Nokaly that LAM, LAE, SAM and SAE are liquid at room temperature and gellify when cooled. Applicant argues that El-Nokaly et al. do not teach the behavior of any amino acid derivatives, far less LAM, LAE, SAM or SAE, inside the body. Applicant argues that the El-Nokaly patent does not teach the use of any amino acid derivatives, much less LAM, LAE, SAM or SAE, to facilitate the release of bioactive substances.

This is not persuasive because El-Nokaly teaches n-acyl amino acid esters that are suitable gelling agents. One of ordinary skill in the art would use these n-acyl amino acid esters in the composition of Fanara, which is a fluid and gels upon contact with mucous membranes. One of ordinary skill in the art would therefore prepare a fluid composition with the n-acyl amino acid esters that would gel upon contact with mucous membranes with a reasonable expectation of success.

Therefore the rejection of 07/17/08 is maintained.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 3-15, 20-21, 23, 26-27, 30-35, and 38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fanara et al. (US 6,464,987) in view of El Nokaly et al. (US 5,843,407).

The claimed invention is a heat-sensitive composition in liquid form, comprising

- a hydrophobic organic liquid,
- an organogelling substance selected from the group consisting of N-lauroyl-L-alanine methyl ester, N-lauroyl-L-alanine ethyl ester, N-stearoyl-L-alanine methyl ester and N-stearoyl-L-alanine ethyl ester, the molecules of which have the capacity to bind together via bonds of low energy, and
- a bioactive substance.

The claimed composition changes to the organogel form during its administration to an animal body and remains in gel form at the body temperature of the animal body.

Fanara teaches pharmaceutical compositions which allow the sustained release of at least one active substance, to methods for preparing these compositions, as well as to their use for administering medicinal products subcutaneously and/or intramuscularly (Col. 1, lines 6-10). "The compositions have the property of gelling instantaneously in the presence of an aqueous phase … upon contact with mucous membranes, a gel forms under the skin or in the muscle, and the medicinal product may diffuse and be released from the gel" (Col. 1, line 65 to Col. 2, line 5). The composition comprises: "a) a therapeutically effective amount of at least one active substance, b) from 3 to 55% by weight of phospholipid, c) from 16 to 72% by weight of pharmaceutically acceptable solvent, and d) from 4 to 52% by weight of fatty acid" (Col. 3, lines 25-35). Active substances include antibiotics, anti-inflammatory agents, peptide active substances such as calcitonin, somatostatin, insulin, bone growth hormone and other growth or repair factors (Col. 3, lines 42-65). The compositions are "fluid

pharmaceutical compositions which are in the form of emulsions, suspensions or oily preparations" (Col. 5, lines 18-20).

Fanara does not expressly teach alanine as an organogelling substance.

El-Nokaly teaches n-acyl amino acid esters as suitable gelling agents (Col. 5, lines 10-14). Oils including triglycerides and plant oils including wheat germ oil, hydrogenated vegetable oils, corn oil, cottonseed oil, olive oil, palm kernel oil, rapeseed oil, safflower oil, jojoba oil, evening primrose oil, avocado oil, and maleated soybean oil (Col. 3, lines 42-60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition that gels instantaneously in the presence of an aqueous phase, upon contact with mucous membranes, as suggested by Fanara, and combine it with the n-acyl amino acid esters that are suitable gelling agents, as suggested by El-Nokaly, and produce the instant invention.

One of ordinary skill in the art would do this because El-Nokaly teaches that n-acyl amino acid esters are suitable gelling agents and can be used with plant oils (Col. 5, lines 10-14 and Col. 3, lines 42-60).

Regarding instant claim 1, the limitation of a heat-sensitive composition would have been obvious over the teaching by Fanara that the compositions gel upon contact with mucous membranes (a gel forms under the skin or in the muscle). The limitation of a composition in liquid form would have been obvious over the fluid compositions taught by Fanara. The limitation of a hydrophobic organic liquid would have been obvious over

the phospholipids (including Phosal 50 PG™ that contains phosphatidylcholine, soybean fatty acids, sunflower monoglycerides, ethanol, propylene glycol and ascorbyl palmitate) taught by Fanara (Col. 5, lines 56-59) and by the triglycerides and plant oils including wheat germ oil, hydrogenated vegetable oils, corn oil, cottonseed oil, olive oil, palm kernel oil, rapeseed oil, safflower oil, jojoba oil, evening primrose oil, avocado oil, and maleated soybean oil taught by El-Nokaly (Col. 3, lines 42-60). The limitation of the organogelling substance which is an amino acid derivative, the molecules of which have the capacity to bind together via bonds of low energy would have been obvious over the n-acyl amino acid esters that are suitable gelling agents, as suggested by El-Nokaly (Col. 5, lines 10-14). The limitation of the bioactive substance would have been obvious over the active substance taught by Fanara (Col. 3, lines 42-65).

Regarding instant claim 3, the limitation of a hydrophilic organic solvent capable of creating weak bonds with the organogelling substance would have been obvious over the ethanol in Phosal 50 PG™ taught by Fanara (Col. 5, lines 56-59).

Regarding instant claims 4-5, the limitation of the organogelling substance having a transition temperature from the liquid state to the gel state which is lower than the temperature of the site of application, and a transition temperature from the gel state to the liquid state that is higher than the body temperature would have been obvious over the teaching of a fluid composition that gels under the skin or muscle for sustained release of an active substance as taught by Fanara. This is because a liquid composition in order to gel under the skin or muscle would intrinsically have a transition temperature (from liquid state to gel state) lower than the temperature of the site of

application. Also, a gel that was implanted in the skin, in order to release an active substance in a sustained or controlled manner, would intrinsically have a transition temperature (from gel state to liquid state) higher than the body temperature, otherwise there would be dose dumping of the active and not the sustained release disclosed by Fanara.

Regarding instant claims 6 and 26, the limitation of the proportion of the hydrophilic organic solvent would have been obvious over the 1.03% ethanol (1. 9% ethanol x 54.6%Phosal 50 PG^{TM}) as taught by Fanara (Col. 6, Table 1).

Regarding instant claims 7-8, the limitation of the hydrophilic organic solvent would have been obvious over the ethanol and propylene glycol (Col. 5, line 61) taught by Fanara.

Regarding instant claims 9-12, and 27, the limitation of the hydrophobic organic liquid would have been obvious over the soybean fatty acids and sunflower monoglycerides taught by Fanara (Col. 5, lines 56-59) and over the triglycerides and plant oils including wheat germ oil, hydrogenated vegetable oils, corn oil, cottonseed oil, olive oil, palm kernel oil, rapeseed oil, safflower oil, jojoba oil, evening primrose oil, avocado oil, and maleated soybean oil taught by El-Nokaly (Col. 3, lines 42-60). One skilled in the art would use different organic liquids or a mixture of different organic liquids during the process of routine experimentation in order to optimize the stability and release profile of the composition and the recited hydrophobic organic liquids would have been obvious variants unless there is evidence of criticality or unexpected results.

Regarding instant claims 13-14, the limitation of the bioactive substance would have been obvious over the peptide active substances such as calcitonin, somatostatin, insulin, and bone growth hormone taught by Fanara (Col. 3, lines 42-65)..

Regarding instant claim 15, the limitation of the percentage of organogelling substance would have been obvious over the 3 to 55% by weight of phospholipid taught by Fanara (Col. 3, lines 25-35) and over the 2% N-lauroyl-L-glutamic acid-di-n-butyl amide gelling agent taught by El-Nokaly (Col. 24, lines 5-8).

Regarding instant claims 30-31, the limitation of the organogelling substance as a molecule of low molecular weight would have been obvious over the n-acyl amino acid esters that are suitable gelling agents, as suggested by El-Nokaly (Col. 5, lines 10-14).

Regarding instant claim 20, the limitation of an organogel remaining stable in gelled form would have been obvious over the gelling composition taught by Fanara, in view of the gelling n-acyl amino acid esters taught by El-Nokaly (Col. 5, lines 10-14).

Regarding instant claims 21 and 32-35, the limitation of a method for administering a bioactive substance to an animal would have been obvious over the composition where a gel forms under the skin or in the muscle taught by Fanara (Col. 1, lines 6-10).

Regarding instant claim 23, the limitation of a process for preparing a composition would have been obvious over the method for preparing a composition where a gel forms under the skin taught by Fanara (Col. 5, lines 29-47).

Regarding instant claim 38, the limitation of a fatty acid ester derivative of alanine would have been obvious over the n-acyl amino acid esters that are suitable gelling agents, as suggested by El-Nokaly (Col. 5, lines 10-14). The limitation of N-lauroyl-L-alanine methyl ester would have been an obvious variant of the n-acyl amino acid esters taught by El-Nokaly unless there is evidence of criticality or unexpected results.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
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